REMARKS

Reconsideration of the present application is respectfully requested. Claims 17-26 are currently pending. Claims 1-16 have been previously canceled without prejudice. Claims 17 and 21 are amended. The amendments to the claims contain no new matter.

I. Rejection of the claims as indefinite

Claims 17-26 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. According to the Examiner, claims 17 and 21 recite the terms "the aqueous fraction," which lacks antecedent basis. Applicant has amended claims 17 and 21 to recite "an aqueous fraction," rendering the rejection moot. Applicant respectfully requests that the rejection be withdrawn.

II. Rejections under 35 U.S.C. § 102(b)

U.S. Patent No. 5,165,938 to Knighton

Claims 17-21 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,165,938 to Knighton (hereafter, "Knighton"). The Examiner contends that Knighton discloses a topical drug composition for wound healing produced from blood comprising microparticles released by collagen and/or thrombin activated platelets into a liquid medium. The Examiner further alleges that the microparticles are separated from the platelets by centrifugation, and mixed with microcrystalline collagens and frozen. Thus, according to the Examiner, the composition of Knighton includes microparticles and extracellular matrix, which allegedly anticipates the claims.

Applicant submits that the claims are directed to a therapeutic composition for promoting wound healing comprising effective amounts of microparticles and one or more added extracellular matrix material, wherein the microparticles are prepared by, among other steps, separating the microparticles from an aqueous fraction of a thrombocyte-free liquid medium. Knighton does not disclose a composition comprising microparticles prepared by separating the microparticles from an aqueous fraction of a thrombocyte-free liquid medium.

Rather, Knighton describes adding thrombin to platelet-rich plasma, whereby the platelet-rich plasma is coagulated and fibrinogen is transformed into insoluble fibrin. Knighton separates the fibrin by centrifugation and discards the fibrin containing sediment. Knighton then mixes the supernatant with a macromolecular substance such as microcrystalline collagen to obtain a paste, which can be applied to wounds. *See, e.g,* Knighton at Col. 3, line 15-Col. 4, line 6. According to Knighton, the supernatant that is mixed to form a paste includes platelet-derived growth factor (PDGF) and platelet-derived angiogenesis factor (PDAF). *See,* Knighton at Col. 3, lines 60-68.

The Examiner contends that the pending claims are product-by-process claims, and the properties of the claimed product are not materially or functionally different than the product disclosed by Knighton. Thus, according to the Examiner, the "aqueous fraction" present in Knighton's product, but not the claimed product, does not patentably distinguish the pending claims. *See,* the Office Action at page 9.

Applicant respectfully disagrees. The Examiner states that the specification as filed provides no specific definitions about the chemical nature/structure or molecular weight of the claimed microparticles. *See,* the Office Action at page 8. Not by way of concession, and solely for the sake of argument, Applicant submits that the claimed composition comprising microparticles and the composition of Knighton are different products due to their different processes of production.

> The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product.

See, e.g., In re Garnero, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979); and M.P.E.P § 2113. The process described by the pending claims is different than the process described by Knighton, and as such, the products prepared according to the two processes are different. For example, by separating the microparticles from an aqueous fraction of a thrombocyte-free liquid medium, as recited by the pending claims, the presently claimed invention provides for a composition comprising microparticles and one or more added extracellular matrix material that can be combined together in a defined ratio. In contrast, Knighton does not separate

microparticles from an aqueous fraction of a thrombocyte-free liquid medium. As described above, Knighton merely adds thrombin to a platelet-rich plasma, which coagulates the platelet-rich plasma and transforms fibrinogen into insoluble fibrin. Knighton then separates the fibrin and coagulated plasma by centrifugation to obtain a supernatant. The supernatant of Knighton would therefore contain proteins and other cellular debris that was not removed with the coagulated plasma and fibrin. Knighton provides no guidance with regard to the amount of microparticles, if any, are present in the supernatant, or how much of the supernatant is occupied by proteins and other cellular debris. As such, an artisan of ordinary skill would have no understanding of how much extracellular matrix to add to the supernatant to create any defined ratios of microparticles : extracellular matrix. For the reasons described above, Applicant asserts that Knighton is not an anticipatory reference, and respectfully requests that the rejection be withdrawn.

U.S. Patent No. 5,185,160 to Chao as evidenced by Exner et al., 2003, Blood Coagulation and Fibrinolysis, 14:773-9

Claims 17-21 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,185,160 to Chao (hereafter, "Chao") as evidenced by Exner et al., 2003, Blood Coagulation and Fibrinolysis, 14:773-9 (hereafter, "Exner"). The Examiner contends that Chao describes a pharmaceutical composition for treating wounds comprising microparticles released from platelets that have been activated by repeated freezing and thawing, wherein the microparticles have been separated from the platelets by centrifugation, and further, have been subjected to virus inactivation by heat. The Examiner relies on Exner for disclosure that freezing-thawing activates platelets. According to the Examiner, the product described by Chao describes the claimed invention.

Applicant respectfully disagrees. Chao does not anticipate the claims because the reference does not describe all the claim elements. Chao describes "platelet membrane microparticles" that are platelet membrane vesicles with procoagulant activity. *See*, Chao at Col. 2, lines 40-50. Chao produces the vesicles from platelet ghosts whose membranes are disrupted, for example, by repeated freeze-thawing or through hypotonic exposure to glycerol. *See, e.g.*, Chao at Col. 4, lines 17-39. However, to generate microparticles, platelets are needed which are intact, not disrupted thrombocyte ghosts, since the excretion of microparticles by thrombocytes

constitutes an active process by the cell. *See*, e.g., Simak and Gelderman, 2006, Transfusion Medicines Reviews. Vol. 20:1-20, cited in the IDS filed 12/7/07, at page 2, "It is important to point out that MP [Microparticle] release is not a random process such as the degradation of the plasma membrane of dying necrotic cells but a highly controlled process associated with different types of cell stimulation." Thus, although Chao may identify its biosubstance as a "microparticle," the biosubstance is produced from disrupted ghost platelets, and as such, is different than the microparticles of the present invention.

Additionally, Applicant submits that the product described by the pending claims is produced by a process that is different than the method of generating a vesicle product from ghost platelets, as described by Chao, and discussed above. Thus, the product prepared according to the process recited by the pending claims is different than the product produced according to Chao's methods. *See,* M.P.E.P. § 2113.

For the reasons described above, Applicant asserts that Chao is not an anticipatory reference, and respectfully requests that the rejection be withdrawn.

III. Rejections under 35 U.S.C. § 103(a)

U.S. Patent No. 5,165,938 to Knighton, U.S. Patent No. 5,185,160 to Chao, U.S. Patent No. 5,552,290 to Michelson et al. and U.S. Patent No. 5,697,980 to Otani et al.

Claims 17-26 stand rejected under 35 U.S.C. § 103(a) as being obvious over Knighton, Chao, U.S. Patent No. 5,552,290 to Michelson et al. (hereafter, "Michelson") and U.S. Patent No. 5,697,980 to Otani et al. (hereafter, "Otani"). The Examiner contends that Knighton and Chao disclose compositions comprising microparticles, as described above. The Examiner now relies on Michelson for its purported disclosure that platelet-derived microparticles are made by activating platelets with various agents, such as collagen, thrombin, ionophore A23187 and protein C5b-9. The Examiner also relies on Otani for its alleged disclosure of filling and prosthetic devices made of titanium, calcium phosphate and organic polymers. According to the Examiner, it would have been obvious to add the microparticles of Knighton and Chao to the medical devices of Otani for the purpose of creating a device for wound healing. Additionally, the Examiner states that it would have been obvious to activate platelets with the platelet

activating agents described by Michelson for the generation of microparticles. Thus, according to the Examiner, the combined disclosure of the cited references describes the claimed invention.

Applicant respectfully disagrees. To support an assertion of obviousness, the Examiner must show that "all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art." M.P.E.P § 2143. *See also KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 127 S. Ct. 1727, 82 (2007).

Applicant submits that the claims are not obvious over the cited references because an artisan of ordinary skill, in view of the combined disclosure of the cited references, would have no reasonable expectation of successfully practicing the claimed invention. As discussed previously, neither Knighton nor Chao suggests or describes a composition comprising microparticles prepared by, among other steps, separating the microparticles from an aqueous fraction of a thrombocyte-free liquid medium, as recited by the pending claims. The Examiner now relies on Michelson for its alleged disclosure of platelet activating agents, and Otani for its alleged disclosure of medical devices. Neither of Michelson nor Otani disclose microparticles as described by the pending claims, and as such, the references do not rectify the failure of Knighton and Chao in describing the claimed invention. For at least this reason, the claims are not obvious over the combined disclosure of the cited references, and Applicant respectfully requests that the rejection be withdrawn.

IV. CONCLUSION

In view of the above amendments and remarks, it is respectfully requested that the application be allowed and passed to issue. If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below. Applicant believes that no fee in addition to the fee associated with the Petition to extend time are due at this time. However, if any other fees are required, the Commissioner is authorized to charge such fees to Deposit Account No. 02-4377.

Respectfully submitted,

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